UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,182	06/24/2003	Robert G. Wisotzkey	R-2243	1519

26619 7590 01/12/2006

JOHN E. BURKE
GREENBERG TRAURIG LLP
1200 17TH STREET, SUITE 2400
DENVER, CO 80202

EXAMINER	
CHEN, SHIN LIN	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,182	WISOTZKEY, ROBERT G.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6-24-03, 2-9-04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I, claims 1-13, in the reply filed on 11-23-05 is acknowledged. The traversal is on the ground(s) that the claimed inventions are closely related with similar functions and uses and the embryonic stem cells comprising a disrupted SLC19A2 gene would not be capable of producing functional protein and it is unclear what target sequence the targeting construct would be used as a probe to identify. Applicant argues that no serious burden is required when search all the groups and a search for one group would also search for another group. This is not found persuasive because of the reasons of record. The targeting vector can have sequence that is homologous to the SLC19A2 gene sequence and a sequence encoding a selectable marker, such as GFP. Therefore, the targeting vector can be used as a probe to identify the SLC19A2 gene or GFP DNA sequence or gene expression, and the embryonic stem cells comprising said targeting vector can be used to produce a recombinant GFP protein. In addition, groups I and II have different classifications. Search for the transgenic mice and a method of making the mice does not require specific search for the targeting vector or embryonic stem cells comprising said vector. They have different classifications and require separate search. Thus, inventions I and II are patentably distinct from each other.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 14 and 15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11-23-05.

Claims 1-15 are pending. Claims 1-13 are under consideration.

Specification

On page 1, line 5, of the specification, the filing date of provisional application 60/391,157 should be June 24, 2002, **NOT 2003**. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "SLC19A2" in claims 1, 11 and 12 is vague and renders the claims indefinite. The term "SLC19A2" is an abbreviation and can stand for various meanings. Spelling out the term "SLC19A2" would be remedial. Claims 2-10 depend from claim 1 and claim 13 depends from claim 12 but fail to clarify the indefiniteness.

5. Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Introducing the murine stem cells into a blastocyst of a donor mouse. In the art of transgenics using homologous recombination in the embryonic stem cells, the selected mouse embryonic stem cells were microinjected into blastocyst of a donor animal and the injected blastocyst is implanted into a pseudopregnant mouse for the development of a transgenic mouse.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to a transgenic mouse comprising a disruption in an endogenous solute carrier family 19 member 2 (SLC19A2 or THTR-1) gene that results in lack of production of functional SLC19A2, wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to wild type mouse, a reproductive system abnormality, such as genitourinary system abnormality, such as abnormality of the testis and epididymus, a cell or tissue obtained from said transgenic mouse, a method of making said transgenic mouse and the transgenic mouse produced by said method.

The specification discloses the nucleotide sequence of SEQ ID No. 1 encoding SLC19A2 gene product, the targeting vector sequence based on the sequence of SEQ ID No. 1, and generation of a transgenic mouse comprising a disruption in an endogenous SLC19A2 gene by using mouse embryonic stem cells via homologous recombination.

The specification provides general assertions that the claimed transgenic mice may be used to identify agents capable of affecting phenotype of a transgenic mouse or to identify

potential therapeutic agents for treating a disease associated with the SLC19A2 gene, or may be used as models for diseases or disorders associated with a disruption in SLC19A2 gene (e.g. p. 4, 19, 20). The specification discloses that homozygous mutant male mice having a disruption in SLC19A2 gene exhibit decreased absolute combined testicular and epididymal organ weights and decreased (organ to weight ratio) combined testicular and epididymal organ weights relative to body weight (Example 4), and exhibit testicular degeneration (degenerative changes of the seminiferous tubules of the testes) and marked hypospermatogenesis. (Example 5).

The asserted utility for the claimed transgenic mice having the recited phenotypes does not appears to be specific and substantial because the evidence of record has not provided any suggestion of a correlation between the recited phenotypes of the claimed transgenic mice, the disruption of the SLC19A2 gene, and a disease or a disorder. The specification fails to provide a correlation between the function of SLC19A2 gene and the recited phenotypes or a correlation between the recited phenotypes and any SLC19A2 related disease or disorder. The asserted utility for the claimed transgenic mouse as a model for a disease or disorder, for identifying agents that affect a phenotype related to the mouse, or for identifying therapeutic agents for treating a disease associated with the SLC19A2 gene does not appears to be specific and substantial because the evidence of record has not provided any suggestion of a correlation between a SLC19A2 gene, the above-recited phenotypes, and any disease or disorder. Therefore, the evidence of record suggests a need to provide independent evidence of an association of the recited phenotypes with a disease or disorder. However, neither the specification nor any art of record provides evidence of the existence of a correlation between the recited phenotypes and a disease or disorder, leaving the skilled artisan to speculate and

investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. Therefore, the utility of identifying agents that affect those phenotypes or a disease associated with the SLC19A2 gene, or the utility for using as a disease model is not apparent.

Diaz et al., 1999 (Nature Genetics, Vol. 22, p. 309-312) states that "[t]hiamine-responsive megaloblastic anaemia syndrome (TRMA;MIM 249270) is an autosomal recessive disorder with features that include megaloblastic anaemia, mild thrombocytopenia and leucopenia, sensorineural deafness and diabetes mellitus". Diaz reports identification and isolation of a new gene, SLC19A2, encoding a thiamine transporter protein of 497 amino acids with 12 transmembrane domains. Two frameshift mutations in exon 2, a 1-bp insertion and a 2-bp deletion are identified in the SLC19A2 gene among four Iranian families with TRMA (e.g. abstract). Oishi et al., 2002 (Human Molecular Genetics, Vol. 11, No. 23, p. 2951-2960) generates Slc19a2-/- mice by disrupting the SLC19A2 gene via homologous recombination in embryonic stem cells and reports that the Slc19a2-/- mutant mice lack high-affinity component of thiamine transport and develop diabetes mellitus with reduced insulin secretion and an enhanced response to insulin when the Slc19a2-/- mice were on a thiamin-free diet. The thiamin-deficient Slc19a2-/- mice also exhibit abnormal bone marrows with a megaloblastosis affecting the erythroid, myeloid and megakaryocyte lines (e.g. abstract). Mutation of SLC19A2 gene was known to be associated with TRMA, however, the phenotypes of the claimed transgenic mice in the instant invention do not appear to be associated with any TRMA syndrome, such as megaloblastic anaemia, mild thrombocytopenia and leucopenia, sensorineural

deafness and diabetes mellitus. The Slc19a2-/- mice generated by Oishi do not show any recited phenotype of the instant claimed invention. There is no evidence of record that shows a correlation between the recited phenotypes, decreased absolute combined testicular and epididymal organ weights and decreased (organ to weight ratio) combined testicular and epididymal organ weights relative to body weight, testicular degeneration, and marked hypospermatogenesis, and the disruption of the endogenous SLC19A2 gene. Thus, the specification fails to establish a correlation between the recited phenotypes and the disruption or function of the endogenous SLC19A2 gene, or a correlation between the recited phenotypes and a particular disease or disorder.

Further, it was known in the art that there is redundancy in the signal transduction pathway within a cell. When expression of a protein is knocked out or the protein is dysfunctional, other protein can compensate the function of said dysfunctional protein. Olsen et al., 2000 (GABA in the Nervous System: the View at Fifty Years/ Editors, David I. Martin, Richard W. Olsen, Chapter 6: Function of GABA Receptors, Insight from Mutant and Knockout Mice, p. 81-95, Lippincott Williams & Wilkins, Philadelphia) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts can lead to embryonic or prenatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (e.g. p. 82, last 11 lines of column 1).

Rescher et al., 2004 (Journal of Cell Science, Vol. 117, p. 2631-2639) reports that annexins are unique membrane binding proteins with diverse functions, for example, annexin can be membrane scaffold proteins, involved in membrane/protein transport, or as an extracellular protein functions as anticoagulant protein, endothelial cell-surface receptor for plasminogen or as anti-inflammatory agent (e.g. abstract, p. 2635, right column, first paragraph). Rescher points out that homozygous annexin A7-/- mice described by Pollard et al., exhibit an embryonic lethal phenotype, whereas annexin A7-/- mice generated by Noegel et al., are viable. Rescher suggests that the difference in the annexin A7-/- mice phenotype could be due to a different genetic background (e.g. p. 2634, left column, first paragraph). Other annexin-knockout mice lacking A1, A2, A5 or A6 do not show obvious phenotype related to a primary defect in vesicle docking and/or fusion event. Rescher reasons that "the annexins targeted in these mice do not serve as essential factors in vesicle docking and/or fusion or that such functions are redundant or taken over by another member of the family during mouse development (e.g. p. 2634, left column, second paragraph).

Thus, knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. Knockout mice with same targeted knockout gene may have different phenotypes, for example, the annexin A7-/- mice discussed above. The resulting phenotype of a knockout gene was unpredictable at the time of the invention, and whether the resulting phenotype is correlated to the disruption of a targeted gene would be unclear without further characterization. Further, using mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype may be a

result of other compensating proteins and not the knocked out gene. There is no evidence of record that correlates the recited phenotypes with the disruption of SLC19A2 gene.

On the other hand, the claims do not specify a particular ES cells and mouse strain used to generate the claimed transgenic mice, therefore, the claims encompass using various ES cells and mouse strains to generate the claimed transgenic mice. The genetic background of the transgenic mice has a large impact on the resulting phenotype of the transgenic mice. The art of transgenics at the time of filing held that the phenotype of transgenic knockout mice was unpredictable. For example, as discussed above, Rescher reasons that the difference in the annexin A7-/- mice phenotype could be due to a different genetic background. Mogil et al., 1999 (Pain, Vol. 80, pages 67-82) reports that there are several limitations to the use of mouse transgenic KO models. Mogil teaches that "the embryonic stem (ES) cell lines used to carry the targeted mutation are all derived from various substrains of the 129 strain" and "it is difficult to separate by homologous recombination the 129-derived transgene from tightly linked gene. Even after repeated backcrosses to C57Bl/6, a step most often omitted in the competition to publish, the wild-type and KO populations will differ in their inheritance of so-called "hitchhiking donor gene" alleles". Knockout mutant mice will inherit alleles tightly linked with the gene disruption, leading to "hitchhiking donor gene" alleles from 129 ES cell lines while the wild-type mice will inherit C57BL/6-derived alleles. "[O]bserved phenotypic differences between wild-type and KO mice could, therefore, be due to the targeted mutation, to allelic variation at one or more of the many unidentified hitchhiking genes, or to an interaction between them" (page 78, left column). In addition, "the background genes from the parent strains can

interact with the targeted mutation ("epistasis"), importantly affecting the observed phenotype" (page 78, left column).

In addition, Sigmund, C., June 2000 (Arterioscler. Thromb. Vasc. Biol., p. 1425-1429), reports that variation in the genetic background contributes to unpredictable resulting phenotypes of transgenic or gene-targeted animals. "Animals containing the same exact genetic manipulation exhibit profoundly different phenotypes when present on diverse genetic backgrounds, demonstrating that genes unrelated, per se, to the ones being targeted can play a significant role in the observed phenotype" (e.g. abstract). Sigmund further states that "many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studies...Although all mouse strains contain the same collection of genes, it is allelic variation...and the interaction between allelic variants that influence a particular phenotype. These "epigenetic" effects can dramatically alter the observed phenotype and therefore can influence or alter the conclusions drawn from experiments" (e.g. introduction). Leonard et al., 1995 (Immunological Reviews, Vol. 148, pages 97-114) disclosed mice with a disruption in the gc gene that was intended to be a model for X-linked severe combined immunodefkiency (XSCID), but display a variety of unexpected traits (abstract). These knockout mice were expected to have thymocytes with decreased proliferation in response to stimulation with antibodies, but the thymocytes proliferated normally (page 105, lines 7-9). In view of the reasons set forth above, it cannot be assumed that the observed phenotypes as claimed in the homozygous mutant male mice as compared to wild-type mice are the result of a SLC19A2 gene disruption as opposed to difference between mouse strains. Absent the correlation between the claimed phenotypes of the mutant mice and the disruption of the SLC19A2 gene and the

correlation between said phenotypes and a particular disease or disorder, one skilled in the art would not know how to use the claimed mutant mice as a disease model, or to identify agents that affect a phenotype related to the mouse, or for identifying therapeutic agents for treating a disease associated with the SLC19A2 gene. Thus, the claimed transgenic mice lack a specific and substantial utility or a well-established utility.

The specification only discloses the phenotypes of the homozygous mutant male mice but fails to disclose any phenotype for the heterozygous mutant mice or homozygous mutant female mice. A transgenic mouse having no phenotype is indistinguishable from a wild-type mouse and does not have a specific and substantial utility or a well-established utility because one skilled in the art would not know where and what to look for in using said transgenic mouse. A substantial utility is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. Absent the phenotype of the claimed transgenic mouse and the correlation between a phenotype of the claimed transgenic mouse and a particular disease or disorder, no "real world" use of the claimed transgenic mouse has been established. Therefore, the claimed transgenic mice lack a specific and substantial or a well-established utility. The evidence of record has not provided any other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and credible.

The cell and tissue of claim 10 are obtained from the claimed transgenic mice. The claimed cell and tissue lack a specific and substantial utility for the reasons set forth above and because the specification does not teach how to use the cell and tissue in any manner other than when they are part of a mouse that is a model of disease or a disorder.

In light of the above, the skilled artisan would not find the asserted utility of the transgenic mice and cells and tissues encompassed by the claims to be specific and substantial or well established.

Claims 1-13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition to the enablement rejection set forth above, the following enablement issues also need to be addressed.

Claims 12 and 13 encompass producing a transgenic mouse comprising a disruption in a SLC19A2 gene by using murine embryonic stem cells. Murine embryonic stem cells include mouse and rat embryonic stem cells.

Houdebine, L-M., 2002 (Journal of Biotechnology, Vol. 98, p. 145-160) states that "animal transgenics is still suffering from technical limitations" (e.g. abstract). Gene replacement by homologous recombination in somatic mammalian cells has relatively poor efficiency and "For unknown reasons, homologous recombination is more frequent in pluripotent embryonic cells" (e.g. p. 148, right column). However, gene transfer or inactivation using embryonic cells has failed in species other than mouse, and "the recombined ES cells have more or less the capacity to participate to the development of chimeric embryos but that transmission of the mutation to progeny has been observed so far only in two mouse lines and essentially of the 129/SV line...The systematic lack of success met in rat, rabbit, chicken, pig, sheep and cow

now inclines to consider that the so- called ES cells cannot be used for the germinal transmission of a mutation except in two mouse lines systematic studies to tentatively identify genes involved in the two mouse lines are in course" (e.g. p. 149, left column). Thus, the claimed method of using murine embryonic stem cells to make mutant mice via homologous recombination at the time of the invention was not enabled other than the use of the two mouse lines mentioned by Houdebine.

In view of the inherent unpredictability of the resulting phenotypes of transgenic mice having a disrupted SLC19A2 gene and the limitation of mouse embryonic stem cells used to make transgenic mice, one skilled in the art at the time of the invention would not know how to make and use the claimed transgenic mice and would require undue experimentation to practice over the full scope of the invention claimed.

Claims 11-13 encompass chimeric mice (genetic mosaics) wherein only a portion of the cells of the mouse comprises the claimed genetic disruption because the claims can be interpreted to read on chimeric mice. The phrase "a transgenic mouse comprising a (heterozygous) disruption in an endogenous SLC19A2 gene" in claims 11 and 12 can be interpreted to read on a chimeric mouse. The specification fails to enable making chimeric mice such that they exhibit any phenotype as encompassed by the claims, including a wild-type phenotype, and the recited phenotypes. The specification teaches generating non-chimeric transgenic mice by using chimeric mice and mating them to C57BL/6 females (page 49, Example 1) to generate non-chimeric transgenic mice. The specification teaches that the non-chimeric transgenic mice whose genome comprises a disruption in the SLC19A2 gene exhibit recited phenotypes as compared to wild-type mice. The specification does not correlate any

phenotype to chimeric mice comprising one or more cells with a disruption in the SLC19A2 gene. The method of making genetic mosaic mice is such that each resulting chimera is comprised of a different, unpredictable ratio of cells of various genotypes. This ratio cannot be predetermined. Furthermore, the spatial distribution of cells of each genotype cannot be predetermined. Therefore, the phenotype of chimeric animals is not only dependent upon the genotype of the cells (which is unpredictable as set forth by the state of the art outlined above, for example see Leonard; Mogil; Sigmund) but is also dependent upon the spatial distribution of the cells and their relative population size. Thus, the phenotype of the chimeric animals encompassed by the claims is highly unpredictable. The specification fails to provide the guidance necessary to overcome this high level of unpredictability to generate a chimeric mouse exhibiting any specific phenotype or any phenotype other than wild type. The specification discloses using the claimed mice as a disease model or for screening for agents that affect the phenotype of the claimed mice. As set forth above, without a predictable phenotype, it would require additional and undue experimentation for one of skill in the art to determine a useful phenotype for the claimed chimeric mice and to determine what to screen for. Therefore, without undue experimentation, the skilled artisan would not know how to use the chimeric mice encompassed by the claims.

For the reasons set forth above, one skilled in the art at the time of the invention would have to engage in undue experimentation to practice over the full scope of the invention claimed. This is particularly true based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, the level of one of

ordinary skill which is high, the amount of experimentation required, and the breadth of the claims.

Claims 12 and 13 encompass using any SLC19A2 gene sequence for the disruption of the mouse SLC19A2 gene. The specification fails to enable using various SLC19A2 gene sequences derived from different organisms for disrupting the mouse SLC19A2 gene in a mouse other than that set forth by SEQ ID No. 1. The breadth of the claims encompasses SLC19A2 genes other than that described and set forth by SEQ ID No. 1. The specification teaches only one SLC19A2 gene (SEQ ID No. 1). The specification fails to teach that other SLC19A2 genes derived from various organisms exist or have the same function as the SLC19A2 gene set forth by SEQ ID No. 1, and fails to teach that those other SLC19A2 gene sequences can be used to disrupt endogenous mouse SLC19A2 gene in making transgenic knockout mice. Therefore, the specification only enables making a transgenic mouse whose genome comprises a disruption of the SLC19A2 gene set forth by SEQ ID No. 1 by using the disclosed SLC19A2 gene sequence.

9. Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 111 1, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

The specification has described the nucleotide sequence, encoding the SLC19A2 gene, as set forth by SEQ ID No. 1. In the instant case the genus of SLC19A2 genes encompassed by the claims lack a written description. The specification fails to describe what DNA molecules other than the nucleotide sequence set forth in SEQ ID No. 1 fall into this genus and it was unknown as of Applicants' effective filing date that any of these DNA molecules would have the property of encoding a SLC19A2 polypeptide having the same structural and functional properties as that encoded by SEQ ID No. 1. There is no evidence on the record of a relationship between the structures of the nucleotide sequences coding for a mouse SLC19A2 gene product and the nucleotide sequence set forth by SEQ ID No. 1 that would provide any reliable information about the structure of DNA molecules within the genus. The claimed invention as a whole is not adequately described if the claims require essential or critical elements that are not adequately described in the specification and that is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor has possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641,1646 (1998).

With the exception of the sequence referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is

not achieved until reduction to practice has occurred regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by any member of the genus of genes encoding a SLC19A2 gene product other than that set forth by SEQ ID No. 1. Therefore, only the SLC19A2 gene encompassed by SEQ ID No. 1, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112 first paragraph. Applicants were not in possession, at the time of the invention, of the transgenic mice generated by using various SLC19A2 gene sequences other than the disclosed sequence of SEQ ID No. 1. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention".

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER